

Inventors: Selsted et al.
Serial No.: 10/009,317
International Filing Date: May 10, 2000
U.S. Entry: November 9, 2001
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REMARKS

New pages 1 through 16 are submitted herewith containing Sequences 1 through 34, formatted in accordance with the conventions set forth in 37 C.F.R. § 1.823. No new matter is introduced by these new pages as they merely represent the sequences originally set forth in the application. The amendments to the specification and claims were made to insert the sequence identification numbers so that they correspond to the Sequence Listing submitted herewith. Accordingly, entry of these amendments and new pages is respectfully requested.

This is the U.S. national stage of international application PCT/US00/12842, filed May 10, 2000. The cover page of the WO publication is attached as Exhibit A.

When the PCT application was filed, the Applicant claimed priority to U.S. application Ser. 09/309,487, filed May 10, 1999. See Exhibit A, item (30).

In addition, the United States was marked in the Request as a designated country with the further indication "continuation-in-part" to reserve the right for the PCT application to be treated as a continuation-in-part of the priority application. See Exhibit A, item (63).

The Applicant hereby amends the application so that it is **not a continuation-in-part application**, and should not be

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treated as such under PCT Rule 4.14. Nevertheless, the Applicant expressly maintains the priority claim to U.S. application Ser. 09/309,487 under PCT Rule 4.10 and PCT Article 8(1).

Accordingly, a patent issuing from this application will have a 20-year patent term based on the international filing date of May 10, 2000.

No fee is deemed necessary in connection with the filing of this Preliminary Amendment. However, if any fee is required, authorization is given to charge the amount of this fee to Deposit Account No. 03-0370.

The Examiner is invited to call the undersigned agent or Cathryn Campbell if there are any questions.

Respectfully submitted,



February 28, 2003
Date

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APPENDIX A

On page 5, please delete the paragraph on lines 14-23 and substitute therefor:

Figure 2 shows the peptide backbone structure of RTD-1. Panel A shows the amino acid sequence of the peptide chain, determined by Edman sequencing. The corresponding MALDI-TOF MS analysis of purified proteolytic fragments is also shown. Residues in parentheses were assigned based on MALDI-TOF MS data. Calculated MALDI-TOF MS values are in parentheses. The peptides shown in Panel A (top to bottom) correspond to SEQ ID NOS:2-9, respectively. Panel B shows a schematic of RTD-1 (SEQ ID NO:1) cyclized peptide backbone.

On page 6, please delete the paragraph on lines 4-12 and substitute therefor::

Figure 4 shows the structure of RTD-1. Panel A shows a schematic of the covalent structure of RTD-1 compared with that of circulin A (SEQ ID NO:10), an antiviral peptide isolated from the plant *Chassalia parvifolia*. Panel B shows a theoretical model of RTD-1 obtained by molecular dynamics and energy minimization in water. The model shows a high degree of structural similarity to porcine protegrin 1 (PG-1; SEQ ID NO:11) for those residues defined in the PG-1 solution structure. Panel

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C shows the alignment of the PG-1 and RTD-1 sequences and disulfide motifs.

On page 8, please delete the paragraph on lines 23-25 and substitute therefor:

Figure 14 shows the DNA probes used for specific hybridization of RTD1a (Panel A; SEQ ID NO:26; complementary sequence, SEQ ID NO:30) and RTD1b (Panel B; SEQ ID NO:27; complementary sequence, SEQ ID NO:31).

On page 9, please delete the paragraph on lines 1-3 and substitute therefor:

Figure 16 shows the sequence and disulfide bonding pattern of RTD-1 (SEQ ID NO:1), RTD-2 (SEQ ID NO:[30]32) and RTD-3 (SEQ ID NO:[31]33).

On page 13, please delete the paragraph on lines 9-18 and substitute therefor:

The invention additionally provides a theta defensin comprising the amino acid sequence Arg-Cys-Ile-Cys-Thr-Arg-Gly-Phe-Cys (SEQ ID NO:18) or Arg-Cys-Leu-Cys-Arg-Arg-Gly-Val-Cys (SEQ ID NO:20). Further provided is a theta defensin having the amino acid sequence Gly-Phe-Cys-Arg-Cys-Ile-Cys-Thr-Arg-Gly-Phe-

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Cys-Arg-Cys-Ile-Cys-Thr-Arg (SEQ ID NO:[30]32). The invention also provides a theta defensin having the amino acid sequence Gly-Val-Cys-Arg-Cys-Leu-Cys-Arg-Arg-Gly-Val-Cys-Arg-Cys-Leu-Cys-Arg-Arg (SEQ ID NO:[31]33).

On page 59, please delete the paragraph on lines 29-31 and on page 60, please delete lines 1-4 and substitute therefor:

In order to understand the transcriptional and translational pathways involved in the production of cyclic RTD-1, the corresponding cDNA was cloned. The finding that RTD-1 is expressed in myeloid cells suggested that its mRNA would be abundant in bone marrow cells. Using rhesus macaque bone marrow mRNA as template, 3' rapid amplification of cDNA ends (RACE) was carried out using degenerate primers corresponding to different 6 or 7 amino acid sequences in the RTD-1 backbone. Polymerase chain reaction (PCR) products were subcloned and sequenced, revealing that portions of the RTD-1 mature peptide sequence were amplified using the degenerate primer corresponding to GVCRCIC (SEQ ID NO:[30]34). The 3' RACE products were then used to probe a rhesus macaque bone marrow cDNA library. Fifteen positive clones were isolated and sequenced, disclosing two very similar cDNAs termed RTD1a and RTD1b.

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In the claims

15. The theta defensin of claim 14, having the amino acid sequence:

Gly-Phe-Cys-Arg-Cys-Ile-Cys-Thr-Arg-Gly-Phe-Cys-Arg-Cys-Ile-Cys-Thr-Arg (SEQ ID NO: [30]32).

19. The theta defensin of claim 14, having the amino acid sequence:

Gly-Val-Cys-Arg-Cys-Leu-Cys-Arg-Arg-Gly-Val-Cys-Arg-Cys-Leu-Cys-Arg-Arg (SEQ ID NO: [31]33).